UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

01/21/00

MEMORANDUM

Subject: D258938
$H_2Orange_2$ Concentrate 117
EPA Registration No. 69268-2

From: Wallace Powell, Biologist
Product Science Branch
Antimicrobials Division (7510C)

Thru: Karen P. Hicks, Team Leader
Chemistry/Toxicology Team
Product Science Branch
Antimicrobials Division (7510C)

Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

To: Marshall Swindell, Product Manager, Team 33
Tony Kish, Team Reviewer, Team 33
Regulatory Management Branch
Antimicrobials Division (7510C)

BACKGROUND

The registrant, Alphen, Inc. (as represented by an agent), has submitted studies for primary eye irritation, primary dermal irritation, acute oral toxicity, and acute dermal toxicity – MRID Nos. 448926-01 through 448926-04, respectively. The studies were submitted in support of a registration amendment for $H_2Orange_2$ Concentrate 117, EPA Registration No. 69268-2, a hard-surface treatment product containing hydrogen peroxide as the active ingredient at 3.95% of the formulation by weight. The registrant wishes to revise the human-hazard and practical-treatment statements on the product label and to change the Signal Word from DANGER to CAUTION. The submitted studies were initially reviewed for Product Science Branch (PSB) by Oak Ridge National Laboratory. The reviews are attached to this memorandum.

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RECOMMENDATION

The submitted studies are acceptable. PSB concurs with the acute Toxicity Categories listed below which were determined in the attached study reviews.

Acute effect	Category
Acute oral toxicity	III – LD_{50} > 2000 mg/kg; this indicates Category III or IV. Category III is assigned for regulatory purposes.
Acute dermal tox.	III – This limit test indicates Category III or IV. Category III is assigned for regulatory purposes.
Primary eye irritation	III
Primary dermal irrit.	IV

The registrant selected $H_2Orange_2$ Super Concentrate 112 (EPA Registration No. 69268-1) as the test material for the dermal irritation, acute oral, and acute dermal toxicity studies. This is acceptable, since that product is more concentrated but otherwise similar to the subject product, and tested out to be non-irritating (Category IV) to the skin and only moderately acutely toxic (Category III) orally and dermally.

The above list of acute Toxicity Categories for the product is incomplete, lacking any reference to acute inhalation or dermal sensitization data or waivers. However, neither the EPA-accepted product label nor the new proposed label nor the registrant's 08/03/99 correspondence makes any reference to inhalation or sensitization. Therefore, the submitted studies are not being reviewed here as a proposed complete data set, but only as support for the label revisions.

PRODUCT LABELING

The following comments apply, in regard to the proposed label of EPA Received date 08/06/99:

1. In the human hazards section, the registrant should delete the statement, "Product, after dilution according to directions, is non-irritating." The phrase "Undiluted product concentrate" should also be deleted from the statement, "Undiluted product concentrate causes moderate eye damage," because the phrase can be taken to imply that the use-dilution is harmless.

   Even though the use-dilution proposed for sanitization is 1:32 by volume, the above text cannot be accepted in the absence of an eye irritation study on the dilution. The results of the submitted eye study on the concentrate are cause for concern. The reason that an eye irritation hazard level as mild as Category III can be assigned to the study is that the observed problems at Day 3 (72 hours) cleared before the Day 7 observation. The problems, however, were significant

and might have persisted at comparable levels for a considerable time after Day 3 (in the absence of further observations recorded before Day 7).

2. In the Practical Treatment section, the registrant should delete the phrase "with product concentrate" from the heading, "In case of CONTACT with product concentrate." No data were submitted or cited to support the concept that the use-dilutions need no practical-treatment statements. Category IV's would have to be assigned across-the-board in order for the full heading to be acceptable.

3. The statements required in the Agency's *Label Review Manual* for the human-hazards section are as follows:

> Causes moderate eye irritation. Harmful if swallowed or absorbed through skin. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling.

Therefore, the following revision (at a minimum) is necessary:

> Add the statement, "Harmful if swallowed or absorbed through skin."

4. The proposed "If swallowed" statements for practical treatment are not the statements indicated by the Agency's *Label Review Manual* for the proposed product. However, ingestion practical-treatment is a controversial topic, and the registrant's proposed statements can be accepted if the registrant considers them to be medically appropriate, and if the registrant adds to them an instruction to "call a physician or poison control center," or to "get medical attention."

DATA EVALUATION REPORT

HYDROGEN PEROXIDE
(ALPHEN H_2 ORANGE 2 SUPER CONCENTRATE 112)

STUDY TYPE: ACUTE ORAL TOXICITY - RAT (81-1)
MRID 44892603; DP BARCODE: 258938

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K116

Primary Reviewer:
Susan Chang, M.S.
Signature: [signature]
Date: SEP 2 8 1999

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.
Signature: [signature]
Date: SEP 2 8 1999

Robert H. Ross, M.S., Group Leader
Signature: [signature]
Date: SEP 2 8 1999

Quality Assurance:
Eric Lewis, M.S.
Signature: [signature]
Date: SEP 2 8 1999

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS 870.1100 [§81-1]

DP BARCODE: D258938 SUBMISSION CODE: S567180
P.C. CODE: 000595 CASE NO.: 062401

TEST MATERIAL: Alphen H_2 Orange 2 Super Concentrate 112 (Hydrogen peroxide)

SYNONYMS: not reported

CITATION: Graver, K. (1999) Acute oral toxicity/LD50 in rats. MB Research Laboratories, 1765 Wentz Road, P.O. Box 178, Spinnerstown, PA 18968. Research Project No. MB 99-7513.01, June 25, 1999. MRID 44892603. Unpublished.

SPONSOR: Alphen, LLC, P.O. Box 19, Maple Grove Road, Georgetown, IL 61846

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44892603) five male and five female fasted young adult Wistar rats per group were given a single oral 2000 mg/kg (Limit test) dose of Alphen H_2 Orange 2 Super Concentrate 112 (Hydrogen peroxide, Batch No. 97334) by gavage and observed for 14 days.

No animals died during the study. Chromorrhinorhea, wet anogenital area, emaciation, few feces, nose/mouth area stained red, lethargy, flaccidity, ataxia, diarrhea, soiling of the anogenital area, and/or dyspnea were noted on some of the rats. All rats had normal body weight gains. Mottled kidneys were noted in two males and two females at necropsy.

The oral LD_{50} for males, females, and combined was > 2000 mg/kg (Limit test).

Alphen H_2 Orange 2 Super Concentrate 112 is in TOXICITY CATEGORY III based on the LD_{50}.

This acute oral study is classified as **Acceptable/guideline** and satisfies the Subdivision F guideline requirements for an acute oral study (81-1) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Alphen H_2 Orange 2 Super Concentrate 112

   Description: clear light yellow liquid
   Lot/Batch #: 97334
   Specific gravity: 1.04
   Composition: not reported

2. Vehicle and/or positive control

   None

3. Test animals

   Species: rat
   Strain: Wistar
   Age and/or weight at dosing: approximately 7-13 weeks; males: 210-235 g, females: 212-233 g
   Source: Ace Animals, Boyertown, PA
   Acclimation period: at least five days
   Diet: fresh Purina Rat Chow No. 5012, *ad libitum*
   Water: *ad libitum*
   Housing: individually in suspended wire cages
   Environmental conditions:
   Temperature: not reported
   Humidity: not reported
   Air changes: not reported
   Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

   Start: April 23, 1999; end: May 7, 1999

2. Animal assignment and treatment

   The study was conducted as a limit test. Following an overnight fast, five rats/sex were given a single 2000 mg/kg dose of the test material by gavage. The animals were observed for clinical signs of toxicity at 1, 2, and 4 hours post dosing and at least once daily for 14 days. Mortality was checked twice daily. They were weighed on study days 0, 7, and 14. All rats were sacrificed and necropsied.

TABLE 1. Doses, mortality/animals treated			
Dose (mg/kg)	Males	Females	Combined
2000	0/5	0/5	0/10

Data taken from p. 7, MRID 44892603.

3. Statistics

Calculation of the oral LD_{50} was not required.

II. RESULTS AND DISCUSSION

A. MORTALITY

No animals died during the study.

The oral LD_{50} for males, females, and combined was > 2000 mg/kg. This places Alphen H_2 Orange 2 Super Concentrate 112 in TOXICITY CATEGORY III.

B. CLINICAL OBSERVATIONS

Chromorrhinorhea was noted from three rats and wet anogenital areas were noted from four rats. Some of the rats had one or more of the following clinical signs: emaciation, few feces, nose/mouth area stained red, lethargy, flaccidity, ataxia, diarrhea, soiling of the anogenital area, and dyspnea. Two rats had no clinical signs during the study.

C. BODY WEIGHT

All rats had normal body weight gains.

D. NECROPSY

Mottled kidneys were noted in two males and two females. All other rats had normal necropsy.

E. DEFICIENCIES

The temperature, humidity, and air change frequency of the animal room were not reported. These would not affect the study results.

DATA EVALUATION REPORT

HYDROGEN PEROXIDE
(ALPHEN H_2 ORANGE 2 SUPER CONCENTRATE 112)

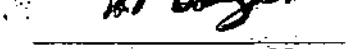
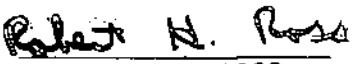
STUDY TYPE: ACUTE DERMAL TOXICITY - RABBIT (81-2)
MRID 44892604; DP BARCODE: 258938

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K116

Primary Reviewer: Susan Chang, M.S.	Signature: Date:	 SEP 28 1999
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.	Signature: Date:	 SEP 28 1999
Robert H. Ross, M.S., Group Leader	Signature: Date:	 SEP 28 1999
Quality Assurance: Eric Lewis, M.S.	Signature: Date:	 SEP 28 1999

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This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

EPA Reviewer: Wallace Powell, ~~Ph.D.~~ _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rabbit
OPPTS 870.1200 [§81-2]

DP BARCODE: D258938 SUBMISSION CODE: S567180
P.C. CODE: 000595 CASE NO.: 062401

TEST MATERIAL: Alphen H_2 Orange 2 Super Concentrate 112 (Hydrogen peroxide)

SYNONYMS: not reported

CITATION: Cerven, D.R. (1999) Acute dermal toxicity in rabbits/LD 50 in rabbits. MB Research Laboratories, 1765 Wentz Road, P.O. Box 178, Spinnerstown, PA 18968. Research Project No. MB 99-7513.02, June 22, 1999. MRID 44892604. Unpublished.

SPONSOR: Alphen, LLC, P.O. Box 19, Maple Grove Road, Georgetown, IL 61846

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44892604) approximately 10% of the body surface area of five male and five female young adult New Zealand White rabbits was dermally exposed to 2000 mg/kg (Limit Test) Alphen H_2 Orange 2 Super Concentrate 112 (Batch No. 97334) for 24 hours. The animals were observed for 14 days.

One male died within one hour of dosing. One female had few feces on day 6. No other clinical toxicity was noted during the study. Dermal irritation (erythema, edema, and/or flaking skin) was noted on all rabbits at 24 hours through day 14. Two surviving males failed to gain weight during the first week of the study. The body weight gains were normal for the other surviving rabbits. Gross necropsy revealed treated skin abnormalities on eight surviving rabbits.

The dermal LD_{50} for males, females, and combined was > 2000 mg/kg (Limit Test).

Alphen H_2 Orange 2 Super Concentrate 112 is in TOXICITY CATEGORY III based on the LD_{50}.

This acute dermal study is classified as **Acceptable/guideline** and satisfies the Subdivision F guideline requirements for an acute dermal study (81-2)in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Alphen H_2 Orange 2 Super Concentrate 112

   Description: clear light yellow liquid
   Lot/Batch #: 97334
   Specific gravity: 1.04
   Composition: not reported

2. Vehicle and/or positive control

   None

3. Test animals

   Species: rabbit
   Strain: New Zealand White
   Age and/or weight at dosing: approximately 12-15 weeks; males: 2.3-2.8 kg, females: 2.1-2.5 kg
   Source: Ace Animals, Boyertown, PA
   Acclimation period: at least five days
   Diet: fresh Purina Rabbit Chow No. 5321
   Water: *ad libitum*
   Housing: individually in suspended wire cages
   Environmental conditions:
   Temperature: not reported
   Humidity: not reported
   Air changes: not reported
   Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

   Start: May 5, 1999; end: May 19, 1999

2. Animal assignment and treatment

   The study was conducted as a limit test using five male and five female rabbits. Animals were given a single 2000 mg/kg dose of Alphen H_2 Orange 2 Super Concentrate 112 applied on top of a gauze patch (10x15 cm) to a clipped area (approximately 10% of the body surface) on the dorsal trunk. The trunk was wrapped with plastic which was secured with tape. The covering was removed 24 hours later and the site washed with distilled water. The test sites were scored for dermal irritation 24 hours after treatment

and on days 7 and 14. The animals were observed for clinical signs of toxicity 1, 2, and 4 hours postdose and once daily thereafter for 14 days. Mortality was checked twice daily. The animals were weighed prior to test material application, and on study days 7 and 14. All rabbits were sacrificed and necropsied.

3. Statistics

Calculation of the dermal LD_{50} was not required.

II. RESULTS AND DISCUSSION

A. MORTALITY

One male died within one hour of dosing.

The dermal LD_{50} for males, females, and combined was > 2000 mg/kg. This places Alphen H_2 Orange 2 Super Concentrate 112 in TOXICITY CATEGORY III.

B. CLINICAL OBSERVATIONS

One female had few feces on day 6. No other clinical toxicity was noted during the study. Very slight to moderate erythema was noted on all rabbits at 24 hours and day 7. By day 14, very slight erythema and moderate erythema were noted on one female and one male, respectively. Slight to severe edema was noted on all rabbits at 24 hours. Very slight and slight edema were noted on seven and one rabbits, respectively, by day 7. Two males had very slight edema by day 14. Flaking skin was noted on most of the rabbits by day 7 through day 14.

C. BODY WEIGHT

Two surviving males failed to gain weight during the first week of the study. The body weight gains were normal for the other surviving rabbits.

D. NECROPSY

Gross necropsy revealed treated skin abnormalities on eight surviving rabbits.

E. DEFICIENCIES

The temperature, humidity, and air change frequency of the animal room were not reported. These would not affect the study results.

DATA EVALUATION REPORT

HYDROGEN PEROXIDE
(ALPHEN H_2 ORANGE 2 SUPER CONCENTRATE 117)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT (81-4)
MRID 44892601; DP BARCODE: 258938

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K116

Primary Reviewer: Susan Chang, M.S.	Signature: Date:	Susan Chang SEP 2 8 1999
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.	Signature: Date:	H T Borges SEP 2 8 1999
Robert H. Ross, M.S., Group Leader	Signature: Date:	Robert H. Ross SEP 2 8 1999
Quality Assurance: Eric Lewis, M.A.	Signature: Date:	Eric B. Lewis SEP 2 8 1999

Disclaimer

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

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EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit
OPPTS 870.2400 [§81-4]

DP BARCODE: D258938 SUBMISSION CODE: S567180
P.C. CODE: 000595 CASE NO.: 062401

TEST MATERIAL: Alphen H_2 Orange 2 Super Concentrate 117 (Hydrogen peroxide)

SYNONYMS: not reported

CITATION: Cerven, D.R. (1999) Acute eye irritation in rabbits. MB Research Laboratories, 1765 Wentz Road, P.O. Box 178, Spinnerstown, PA 18968. Research Project No. MB 98-7280.04, February 22, 1999. MRID 44892601. Unpublished.

SPONSOR: Alphen, LLC, P.O. Box 19, Maple Grove Road, Georgetown, IL 61846

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 44892601) 0.1 mL of Alphen H_2 Orange 2 Super Concentrate 117 (Batch No. 97297) was instilled into the conjunctival sac of three female New Zealand white rabbits. The contralateral eye of the rabbit served as control. The eyes were scored for ocular irritation according to the Draize method 1, 24, 48, and 72 hours after instillation and on day 7.

Corneal opacity was noted on 1/3 rabbits 24 hours after test material instillation and persisted through 72 hours before resolution by day 7. Iritis was noted on 3/3 rabbits one hour after test material instillation with resolution on one rabbit by 48 hours and on two rabbits by day 7. The test material induced conjunctival redness and chemosis one hour through 72 hours after test material instillation with resolution by day 7. Conjunctival discharge was noted on all rabbits one hour after test material instillation with resolution by day 7. The highest total ocular irritation index was 21.67 recorded 24 hours after test material instillation.

In this study, Alphen H_2 Orange 2 Super Concentrate 117 was mildly irritating and is in TOXICITY CATEGORY III for primary eye irritation.

This study is classified as **Acceptable/guideline** and satisfies the Subdivision F guideline requirements for a primary eye irritation study (81-4) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

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I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Alphen H_2 Orange 2 Super Concentrate 117

   Description: clear colorless liquid
   Lot/Batch #: 97297
   Composition: not reported

2. Vehicle

   None

3. Test animals

   Species: rabbit
   Strain: New Zealand white
   Age and weight at dosing: approximately 13-15 weeks; females: 2.0-2.4 kg
   Source: Ace Animals, Boyertown, PA
   Acclimation period: at least five days.
   Diet: fresh Purina Rabbit Chow No. 5321
   Water: *ad libitum*
   Housing: individually in suspended cages
   Environmental conditions:
   Temperature: not reported
   Humidity: not reported
   Air changes: not reported
   Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

   Start: December 7, 1998; end: December 14, 1998

2. Animal assignment and treatment

   The test material (0.1 mL) was instilled into the conjunctival sac of three female rabbits and the eye lids held together briefly. The contralateral eye of each rabbit served as control. The treated eyes of the rabbits were examined with sodium fluorescein at 24, 48, and 72 hours and on day 7. The animals were scored for ocular irritation 1, 24, 48, and 72 hours after instillation and on day 7 according to the Draize method.

II. RESULTS AND DISCUSSION

A. Corneal opacity was noted on 1/3 rabbits 24 hours after test material instillation and persisted through 72 hours before resolution by day 7. Iritis was noted on 3/3 rabbits one hour after test material instillation with resolution on one rabbit by 48 hours and on two rabbits by day 7. The test material induced conjunctival redness (grade 1-3) and chemosis (grade 1-4) one hour through 72 hours after test material instillation with resolution by day 7. Conjunctival discharge was noted on all rabbits one hour after test material instillation with resolution by day 7. The highest total ocular irritation index was 21.67 recorded 24 hours after test material instillation.

This classifies the test material as mildly irritating. Alphen H_2 Orange 2 Super Concentrate 112 is in TOXICITY CATEGORY III.

B. DEFICIENCIES

The temperature, humidity, and air change frequency of the animal room were not reported. These would not affect the study results.

DATA EVALUATION REPORT

HYDROGEN PEROXIDE
(ALPHEN H_2 ORANGE$_2$ SUPER CONCENTRATE 112)

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT (81-5)

MRID 44892602; DP BARCODE: 258938

Prepared for

Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by

Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K116

Primary Reviewer: Susan Chang, M.S.	Signature: Date:	SEP 2 8 1999
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.), Ph.D., D.A.B.T.	Signature: Date:	SEP 2 8 1999
Robert H. Ross, M.S., Group Leader	Signature: Date:	SEP 2 8 1999
Quality Assurance: Eric Lewis, M.S.	Signature: Date:	SEP 2 8 1999

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

EPA Reviewer: Wallace Powell, Ph.D. _____, Date _____
EPA Work Assignment Manager: Nader Elkassabany, Ph.D. _____, Date _____

DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit
OPPTS 870.2500 [§81-5]

DP BARCODE: D258938
P.C. CODE: 000595

SUBMISSION CODE: S567180
CASE NO.: 062401

TEST MATERIAL: Alphen H_2 Orange$_2$ Super Concentrate 112 (Hydrogen peroxide)

SYNONYMS: not reported

CITATION: Cerven, D.R. (1999) Acute dermal irritation in rabbits. MB Research Laboratories, 1765 Wentz Road, P.O. Box 178, Spinnerstown, PA 18968. Research Project No. MB 98-7182.03, February 22, 1999. MRID 44892602. Unpublished.

SPONSOR: Alphen, LLC, P.O. Box 19, Maple Grove Road, Georgetown, IL 61846

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 44892602) six female adult New Zealand white rabbits were dermally exposed on the dorsal trunk to 0.5 mL Alphen H_2 Orange$_2$ Super Concentrate 112 (Batch No. 97293) for 4 hours. The animals were observed for 72 hours. Irritation was scored by the method of Draize.

No irritation was noted on any rabbit during the study.

In this study, Alphen H_2 Orange$_2$ Super Concentrate 112 was not an irritant and is in TOXICITY CATEGORY IV for primary dermal irritation.

This study is classified as **Acceptable/guideline** and satisfies the Subdivision F guideline requirements for a primary dermal irritation study (81-5) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Alphen H_2 Orange$_2$ Super Concentrate 112

   Description: clear light yellow liquid
   Lot/Batch #: 97293
   Composition: not reported

2. Vehicle

None

3. Test animals

Species: rabbit
Strain: New Zealand white
Age and weight at dosing: approximately 12-17 weeks; males: 2.6-2.9 kg, female: 2.8 kg
Source: Ace Animals, Boyertown, PA
Acclimation period: at least 5 days
Diet: fresh Purina Rabbit Chow No. 5321
Water: *ad libitum*
Housing: individually in suspended wire cages
Environmental conditions:
Temperature: not reported
Humidity: not reported
Air changes: not reported
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Start: October 27, 1998; end: November 6, 1998

2. Animal assignment and treatment

One female and two male animals were given a single 0.5 mL dose of Alphen H_2 Orange$_2$ Super Concentrate 112 applied under a 2.5x2.5 cm gauze patch on the clipped dorsal trunk. Thepatch was secured with tape and the trunk was wrapped with plastic in a semi-occlusive manner. The dressings were left in place for 4 hours, after which they were removed and the application sites washed with distilled water. The site was scored for erythema and edema according to the Draize method 60 minutes, 24, 48, and 72 hours after patch removal.

II. RESULTS AND DISCUSSION

A. No irritation was noted on any rabbit during the study.

Alphen H_2 Orange$_2$ Super Concentrate 112 was not an irritant and is in TOXICITY CATEGORY IV.

B. DEFICIENCIES

The temperature, humidity, and air change frequency of the animal room were not reported. These would not affect the study results.